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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,159	06/26/2007	Carsten Hopf	50125/113001	5292
21559	7590	11/27/2009	EXAMINER	
CLARK & ELBING LLP 101 FEDERAL STREET BOSTON, MA 02110				WANG, CHANG YU
ART UNIT		PAPER NUMBER		
		1649		
NOTIFICATION DATE			DELIVERY MODE	
11/27/2009			ELECTRONIC	

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/587,159	HOPF ET AL.	
	Examiner	Art Unit	
	CHANG-YU WANG	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 05 August 2009.
 2a) This action is **FINAL**. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-12 is/are pending in the application.
 4a) Of the above claim(s) 1-6, 11 and 12 is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 7-10 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on 7/25/06 is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) Notice of References Cited (PTO-892)
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
 3) Information Disclosure Statement(s) (PTO/SB/08)
 Paper No(s)/Mail Date _____.
 4) Interview Summary (PTO-413)
 Paper No(s)/Mail Date _____.
 5) Notice of Informal Patent Application
 6) Other: _____.

DETAILED ACTION
Status of Application/Election/Restrictions

1. Applicant's election without traverse of Group II (claims 7-10) in the reply filed on 8/5/09 is acknowledged.

Claims 1-12 are pending. Claims 13-17 are canceled. Claims 1-6 and 11-12 are withdrawn without traverse (filed 8/5/09) from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 8/5/09. Claims 7-10 are under examination in this office action.

Drawings

2. The drawing/figure (Figure 3) is objected to because tables and sequence listings included in the specification must not be duplicated in the drawings. See 37 C.F.R. §1.58(a) and §1.83. Appropriate correction is required.

See MPEP 608.02 [R-3]-I Drawing requirements

If the specification includes a sequence listing or a table, such a sequence listing or table is not permitted to be reprinted in the drawings. 37 CFR 1.83(a) and 1.58(a).

Specification

3. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that

the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The abstract of the disclosure is objected to because it contains more than 150 words and more than one paragraph. Correction is required. See MPEP § 608.01(b).

4. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Note that the elected invention is directed to a method of identifying a gamma/beta secretase modulator by identifying a GPR49-interacting molecule.

Claim Objections

5. Claims 7-10 are objected to because of the following informalities: GPR49 and APP are not a common abbreviation in the art. Applicants are required to spell out GPR49 and APP at the first usage. Appropriate correction is required.

In addition, claim 7 is objected to because of the recitation of "identifying of a GPR49-interacting.....", which is grammatically awkward. Further, claim 10 is objected to because of the recitation "Abeta42". Based on the specification, Abeta42 should be Abeta1-42 peptide. Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention. \

Claims 7-9 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: how to detect and what gamma/beta secretase activity is to be evaluated.

Claims 7-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 7-10 are indefinite because the terms “GPR49” and “APP” are recited in the claims without a reference to a precise amino acid sequence identified by a proper SEQ ID NO: or providing a full name for abbreviated names. Without identification of property or combination of properties which are unique to and, therefore, definitive of the instant recitations, the metes and bounds of the claims remain undetermined. Further, the use of laboratory designations only to identify a particular molecule renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct molecules. The rejection can be obviated by amending the claims to specifically and uniquely identify GPR49 and APP, for example, by SEQ ID NO: and function of GPR49.

In addition, claims 7-8 and 10 are indefinite because of the recitation “modulator” or “modulating”. Applicant fails to define the word “modulator” or “modulating” recited in

the claims. A compound can either enhance or inhibit binding or activity of a GPR49-interacting molecule. Since the claims fail to define what activity of GPR49 or gamma/beta secretase activity is, it is unclear how a compound can modulate gamma/beta secretase activity, which renders the claims indefinite.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for identifying a GPR49-interacting molecule by determining whether a test compound is able to bind to GPR49 (SEQ ID NO:2) and determine whether the test compound can enhance or inhibit the GPR49 gamma/beta secretase activity to cleave APP into Abeta1-42, does not reasonably provide enablement for identifying an undefined gamma/beta secretase modulator by identifying a GPR49-interacting molecule using all of structural and functional GPR49 proteins that are not structurally and functionally defined and with no defined activity as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

“There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the

enablement requirement and whether any necessary experimentation is ‘undue’. These factors include, but are not limited to: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)”. See MPEP § 2164.01.

Claims 7-10 are drawn to a method for identifying a gamma-secretase and/or a beta secretase modulator, comprising the following steps: a) identifying a GPR49-interacting molecule by determining whether a given test compound is a GPR49-interacting molecule, b) determining whether the GPR49-interacting molecule of step a) is capable of modulating gamma-secretase and/or beta-secretase activity. Dependent claim 9 is directed to the interaction of the test compound with GPR49 resulting in an inhibition of GPR49 activity and dependent claim 10 is directed to measuring the gamma/beta secretase activity to cleave APP by detecting the production of Abeta 42 peptide. The claims encompass the use of the structurally and functionally undefined GPR49 proteins. The claims also encompass screening undefined modulators and detecting undefined gamma/beta activity.

The instant invention is based on the finding that siRNA targeting GPR49 caused significant attenuation of Abeta1-42 secretion. The specification shows that siRNA targeting GPR49 caused significant attenuation of Abeta1-42 secretion in SKNBE2 cells

stably overexpressing human APP695 by detecting the levels of Abeta1-42 by ELSA but not Luc3 siRNA. The specification also shows that heterologous expression of GPR49 causes constitutive increases in cellular cAMP levels. Applicant extrapolates the above findings to the claimed method to identify a gamma/beta secretase modulator by identifying a GPR49-interacting molecule that modulates gamma/beta secretase activity.

Based on the specification and the prior art, Applicant is enabled for a method for identifying a GPR49-interacting molecule by determining whether a test compound is able to bind to GPR49 (SEQ ID NO:2) and determine whether the test compound can enhance or inhibit the GPR49 gamma/beta secretase activity on cleavage of APP into Abeta1-42. In addition, Applicant is also enabled for a method of identifying a GPR49-interacting molecule that inhibits or enhances the intracellular cAMP levels as taught by the issued patents NOS. US6555339, 7189539, 7339032 & 7410777. However, the claims are not limited to the method as set forth above.

Based on the specification on p. 4-6, the definition of GPR 49 encompasses structurally and functionally undefined functionally active derivatives, fragments, homologues and variants (see p. 4-6). However, the specification fails to provide sufficient guidance to enable a skilled artisan to practice the claimed invention in its full scope. The specification fails to teach what other common structures and amino acid sequences are required by all of the GPR49 proteins including derivatives, variants and homologues. It is known in the art that an amino acid modification on a molecule can abolish the activity of the molecule. For example, a substitution of lysine residue by glutamic acid at position 118 of acidic fibroblast growth factor results in a substantial

loss of its biological activity including the binding ability to heparin and its receptor (Burgess et al. J of Cell Bio. 1990, 111:2129-2138). Although many amino acid substitutions are possible in any given protein, the position of where such amino acid substitutions can be made is critical for maintaining the function of a protein; i.e. only certain positions can tolerate conservative substitutions without changing the relationship of three dimensional structure and function of the protein (col 2, p. 1306, Bowie et al. Science, 1990, 247:1306-1310). Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would not immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active because conformation is dependent upon surrounding residues; i.e. substitution of non-essential residues can often destroy activity. In addition to a core determinant sequence, the protein-protein interaction also relies on the flanking or noncontiguous residues (see p. 445 the second column, first paragraph, Pawson et al. 2003, Science 300:445-452). The optimal binding motif for a domain is not necessarily suitable for physiological or in vivo interaction. The predictive data always need to be validated by actual analyses in cells (see p. 445, the third column, second paragraph, Pawson et al. 2003, Science 300:445-452). The instant specification fails to teach what specific or commons structures/amino acid sequences can or cannot be included/changed in all GPR45 proteins in order to preserve the activity of SEQ ID NO:2 in cleavage of APP into Abeta1-42. In addition, neither the specification nor the prior art teaches what specific structures/characteristics are required for the claimed molecules to preserve any GPR49 gamma/beta secretase

activity and thereby to be used in the claimed method. Thus, a skilled artisan cannot contemplate how to make and use the claimed GPR49 proteins in the claimed method.

Further, the specification only describes gamma/beta secretase activity of cleavage on APP into Abeta1-42. The specification fails to provide sufficient guidance to enable a skilled artisan to practice the claimed invention by detecting all of gamma/beta secretase activities on undefined or unknown substrates. The specification also fails to teach how to determine whether a test compound can be considered as a modulator since the specification fails to define how a test compound can modulate gamma/beta secretase activity or GPR49 activity.

Moreover, based on the specification, the definition of "activity" refers to the function of a molecule including but not limited to biological chemical, physical.....enzymatic activity, interacting with other molecule... (see p.5). Although the specification describes possible general activities for GPR49, the specification fails to provide sufficient guidance to enable a skilled artisan to detect and measure all of GPR49 activities and all of gamma/beta activities on undefined substrates or molecule. The specification fails to provide information on what other specific activities of GPR45 are and thereby can be used to determine gamma/beta secretase activity and further to identify a gamma/beta secretase modulator. The specification also fails to teach the relationship between the detection of the intracellular cAMP levels and all of the gamma/beta secretase activities and all of GPR49 activities. Since the relationship between the decreased or increased levels of cAMP and the activity of GPR49 or gamma/secretase activity on undefined substrates is unknown, a skilled artisan cannot

contemplate how to use the claimed method to detect all of undefined GPR49 activities and gamma/beta secretase activities without knowing their specific substrates.

Therefore, in view of the necessity of experimentation, the limited working examples, the unpredictability of the art, and the lack of sufficient guidance in the specification, undue experimentation would be required by a skilled artisan to perform in order to practice the claimed invention as it pertains to the method for identifying a gamma/beta secretase modulator by identifying whether a test compound is a GPR49-interacting molecule.

8. Claims 7-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

Claims 7-10 are drawn to a method for identifying a gamma-secretase and/or a beta secretase modulator, comprising the following steps: a) identifying a GPR49-

interacting molecule by determining whether a given test compound is a GPR49-interacting molecule, b) determining whether the GPR49-interacting molecule of step a) is capable of modulating gamma-secretase and/or beta-secretase activity. Dependent claim 9 is directed to the interaction of the test compound with GPR49 resulting in an inhibition of GPR49 activity and dependent claim 10 is directed to measuring the gamma/beta secretase activity to cleave APP by detecting the production of Abeta 42 peptide. The claims encompass the use of a genus of GPR49 proteins to identify a undefined gamma/beta secretase modulator. The claims 7-9 also encompass detecting and measuring a genus of gamma/beta secretase activity and GPR49 activity.

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant is in possession of and what Applicant is claiming. From the specification, it is clear that Applicant is in possession of the use of GPR49 having the amino acid sequence of SEQ ID NO:2 and in possession of detecting and measuring the gamma/beta secretase activity to cleave APP into Abeta42. However, the claims are not limited to the molecule and the activity as set forth above. Based on the specification the definition of GPR 49 encompasses structurally and functionally undefined functionally active derivatives, fragments, homologues and variants (see p. 4-6). Although the specification describes several possible functionally active derivatives, homologues and variants, Applicant is not in possession of other GPR49 proteins as described in the specification to be used in the claimed method. There is no identification of any particular portion of the structure that must be conserved for the

claimed genus of GPR49 proteins. The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of GPR49 proteins. There is no description of the conserved regions which are critical to the function of the claimed genus. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure of other GPR49 proteins to the function of GPR49 having the amino acid sequence of SEQ ID NO:2. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify what other GPR49 proteins might be. Since the common characteristics/features of other GPR49 proteins are unknown, a skilled artisan cannot envision the functional correlations of the claimed genus with the claimed invention.

In addition, based on the specification, the definition of "activity" refers to the function of a molecule including but not limited to biological chemical, physical.....enzymatic activity, interacting with other molecule... (see p.5). Although the specification describes possible general activity, Applicant is not in possession of detecting these non-specific activities as described in the specification in the claimed method. The specification fails to provide information on what other specific activities of GPR45 are and thereby can be used to determine gamma/beta secretase activity and to identify a gamma/beta secretase modulator. The specification only describes gamma/beta secretase cleavage on APP into Abeta1-42.

Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the genus of proteins.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF’s were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, a method for identifying a gamma/beta secretase modulator by identifying whether a test compound is a GPR49-interacting molecule has not met the

written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement. See MPEP § 2163.

Conclusion

9. NO CLAIM IS ALLOWED.

10. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

SEQ ID NO:1

AFU03352
ID AFU03352 standard; DNA; 21 BP.
AC AFU03352;
DT 01-MAY-2008 (first entry)
DE GPR49 oligonucleotide, SEQ ID 17500.
KW G protein-coupled receptor 49; GPR49; Cytostatic; Vaccine; colon tumor;
KW ss.
OS Homo sapiens.
PN US2004265230-A1.
PD 30-DEC-2004.
PF 06-JAN-2004; 2004US-00751736.
PR 06-JAN-2003; 2003US-0438000P.
PA (MART/) MARTINEZ R V.
PA (BROW/) BROWN E L.
PA (LIUW/) LIU W.
PI Martinez RV, Brown EL, Liu W;
DR WPI; 2004-553385/53.
PT Diagnosing or treating colon cancer, comprises detecting a level of a

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PT polypeptide encoded by a colon cancer gene or an expression profile of
 PT colon cancer genes in a biological sample and comparing it with a
 PT control.
 PS Claim 16; SEQ ID NO 17500; Opp; English.
 CC The present invention relates to a method for diagnosing or treating
 CC colon cancer. The method comprises detecting a level of a polypeptide
 CC encoded by a colon cancer gene or an expression profile of colon cancer
 CC genes in a biological sample and comparing it with a control. The methods
 CC are useful for diagnosing, monitoring, preventing and treating colon
 CC cancer. The colon cancer genes and their encoded products are useful as
 CC markers or prophylactic or therapeutic agents for detecting or treating
 CC colon cancer. GPR49 (G protein-coupled receptor 49) is an orphan-G protein
 CC -coupled receptor with an unknown ligand. Expression of GPR49 gene has
 CC been reported in brain, skeletal muscle, placenta, and spinal cord. The
 CC present sequence is an oligonucleotide for which short interfering RNA
 CC (siRNA) oligonucleotides can be designed for inhibiting gene expression.
 CC Note: The sequence data for this patent did not form part of the printed
 CC specification but was obtained in electronic format directly from USPTO
 CC at seqdata.uspto.gov/sequence.html.
 SQ Sequence 21 BP; 7 A; 5 C; 5 G; 4 T; 0 U; 0 Other;

Query Match 100.0%; Score 21; DB 2; Length 21;
 Best Local Similarity 100.0%; Pred. No. 1.6;
 Matches 21; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
 Qy 1 AACAGCAGTATGGACGACCTT 21
 |||||||
 Db 1 AACAGCAGTATGGACGACCTT 21

SEQ ID NO:2

US-09-170-496D-264
 ; Sequence 264, Application US/09170496D
 ; Patent No. 6555339
 ; GENERAL INFORMATION:
 ; APPLICANT: Behan, Dominic P.
 ; APPLICANT: Chalmers, Derek T.
 ; APPLICANT: Liaw, Chen W.
 ; TITLE OF INVENTION: No. 6555339-Endogenous, Constitutively Activated Human G Protein-Coupled
 ; TITLE OF INVENTION: Receptors
 ; FILE REFERENCE: AREN-0040
 ; CURRENT APPLICATION NUMBER: US/09/170,496D
 ; CURRENT FILING DATE: 1998-10-13
 ; NUMBER OF SEQ ID NOS: 294
 ; SOFTWARE: PatentIn version 3.1
 ; SEQ ID NO 264
 ; LENGTH: 907
 ; TYPE: PRT
 ; ORGANISM: Homo sapiens
 US-09-170-496D-264

Query Match 100.0%; Score 4702; DB 2; Length 907;
 Best Local Similarity 100.0%; Pred. No. 0;
 Matches 907; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
 Qy 1 MDT SRLGVLLSLPVLLQLATGGSSPRSGVLLRGCPTHCHCEPDGRMLLRVDCSDLGLSEL 60
 |||||||
 Db 1 MDT SRLGVLLSLPVLLQLATGGSSPRSGVLLRGCPTHCHCEPDGRMLLRVDCSDLGLSEL 60
 Qy 61 PSNL SVFTSYLDLSMNNISQLLPNPLPSLRFLEELRLAGNALTYIPKGAFTGLYSLKVL M 120
 |||||||
 Db 61 PSNL SVFTSYLDLSMNNISQLLPNPLPSLRFLEELRLAGNALTYIPKGAFTGLYSLKVL M 120
 Qy 121 LQNNQLRHVPTEALQNLRLSLSRLDAHISYVPPSCFSGLHSLRHLWLDDNALTEIPVQ 180
 |||||||

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Db      121  LQNNQLRHVPTEALQNLRSLQSLRLDANHISYVPPSCFSGLHSLRHLWLDNALTIEIPVQ 180
Qy      181  AFRSLSLQAMTLALNKIHIPDYAFGNLSSLVVLHLHNNRIHSLGKCFDGLHSLETLD 240
Db      181  AFRSLSLQAMTLALNKIHIPDYAFGNLSSLVVLHLHNNRIHSLGKCFDGLHSLETLD 240
Qy      241  LNYNNLDEFPTAIRTLSNLKELGFHSNNIRSIPEKAFVGNPSSLITIHFYDNPIQFVGRSA 300
Db      241  LNYNNLDEFPTAIRTLSNLKELGFHSNNIRSIPEKAFVGNPSSLITIHFYDNPIQFVGRSA 300
Qy      301  FQHLPELRTLTLNGASQITEFPDLTGTANLESLTGQAQISSLPQTVCNQLPNLQVLDLS 360
Db      301  FQHLPELRTLTLNGASQITEFPDLTGTANLESLTGQAQISSLPQTVCNQLPNLQVLDLS 360
Qy      361  YNLLEDLPSFSVCQKLQKIDLRHNEIYEIKVDTFQQLLSSLRSLNLAWNKIAIIHPNAFST 420
Db      361  YNLLEDLPSFSVCQKLQKIDLRHNEIYEIKVDTFQQLLSSLRSLNLAWNKIAIIHPNAFST 420
Qy      421  LPSLIKLDLSSNLSSFPITGLHGLTHLKLGNHALQSLISSENFPELKVIEMPTYAYQCC 480
Db      421  LPSLIKLDLSSNLSSFPITGLHGLTHLKLGNHALQSLISSENFPELKVIEMPTYAYQCC 480
Qy      481  AFGVCENAYKISNQWNKGDNSSMDDLHKKDAGMFQAQDERDLEDFLLDFEEDLKALHSQ 540
Db      481  AFGVCENAYKISNQWNKGDNSSMDDLHKKDAGMFQAQDERDLEDFLLDFEEDLKALHSQ 540
Qy      541  CSPSPGPFPKPCHEHLLDGWLIRIGVWTIAVLALTNCALVTSTVFRSPLYISPICKLIGVIA 600
Db      541  CSPSPGPFPKPCHEHLLDGWLIRIGVWTIAVLALTNCALVTSTVFRSPLYISPICKLIGVIA 600
Qy      601  AVNMLTGVSSAVLAGVDAFTFGSFARHGAWWENGVGCHVIGFLSIFASESSVFLLTLAAL 660
Db      601  AVNMLTGVSSAVLAGVDAFTFGSFARHGAWWENGVGCHVIGFLSIFASESSVFLLTLAAL 660
Qy      661  ERGFSVKYSAKFETKAPFSSLKVIILLCALLALTMAAVPLLGGSKYGASPLCLPLPFGE 720
Db      661  ERGFSVKYSAKFETKAPFSSLKVIILLCALLALTMAAVPLLGGSKYGASPLCLPLPFGE 720
Qy      721  STMGYMVALILLNSLCFLMMTIAYTKLYCNLDKGDLENIWDCSMVKHIALLLFTNCILNC 780
Db      721  STMGYMVALILLNSLCFLMMTIAYTKLYCNLDKGDLENIWDCSMVKHIALLLFTNCILNC 780
Qy      781  PVAFLSFSSLINLTFSPEVIKFILLVVVPLPACLNPLLYILFNPHFKEDLVSRLKQTYV 840
Db      781  PVAFLSFSSLINLTFSPEVIKFILLVVVPLPACLNPLLYILFNPHFKEDLVSRLKQTYV 840
Qy      841  WTRSKHPSLMSINSDDVEKQSCDSTQALVTFTSSSITYDLPSSVPSPAYPVTECHLSS 900
Db      841  WTRSKHPSLMSINSDDVEKQSCDSTQALVTFTSSSITYDLPSSVPSPAYPVTECHLSS 900
Qy      901  VAFVPCL 907
Db      901  VAFVPCL 907

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ABP81968

ID ABP81968 standard; protein; 907 AA.

AC ABP81968;

DT 15-JUN-2007 (revised)

DT 04-MAR-2003 (first entry)

DE Human G protein-coupled receptor GPR49 protein SEQ ID NO:422.

KW G protein-coupled receptor; GPCR; antigenic peptide; gene therapy;

KW G protein-coupled receptor modulator; antibody; immune-related disease;

KW growth-related disease; cell regeneration-related disease; AIDS; cancer;

KW immunological-related cell proliferative disease; autoimmune disease;

KW Alzheimer's disease; atherosclerosis; infection; osteoarthritis; allergy;

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KW osteoporosis; cardiomyopathy; inflammation; Crohn's disease; diabetes; KW graft versus host disease; Parkinson's disease; multiple sclerosis; pain; KW psoriasis; anxiety; depression; schizophrenia; dementia; memory loss; KW mental retardation; epilepsy; asthma; tuberculosis; obesity; nausea; KW hypertension; hypotension; renal disorder; rheumatoid arthritis; trauma; KW ulcer; BOND_PC;
 KW leucine-rich repeat-containing G protein-coupled receptor 5;
 KW orphan G protein-coupled receptor HG38; G protein-coupled receptor 67;
 KW G protein-coupled receptor 49; LGR5; FEX; HG38; GPR67; GRP49; GPR49;
 KW GPR67, GPR49; LGR5 protein; MGC117008;
 KW orphan G protein-coupled receptor HG38 [Homo sapiens]; G04872; G05515;
 KW G05887; G07165; G07186; G016020; G016021; G016500.
 OS Homo sapiens.
 PN WO200261087-A2.
 PD 08-AUG-2002.
 PF 19-DEC-2001; 2001WO-US050107.
 PR 19-DEC-2000; 2000US-0257144P.
 PA (LIFE-) LIFESPAN BIOSCIENCES INC.
 PI Burmer GC, Roush CL, Brown JP;
 DR WPI; 2003-046718/04.
 DR N-PSDB; ABZ42816.
 DR PC:NCBI; gi4504379.
 DR PC:SWISSPROT; O75473.
 PT New isolated antigenic peptides e.g., for G protein-coupled receptors (GPCR), useful for diagnosing and designing drugs for treating conditions in which GPCRs are involved, e.g. AIDS, Alzheimer's disease, cancer or PT autoimmune diseases.
 PS Disclosure; Fig 1; 523pp; English.
 CC The present invention describes antigenic peptides (I) comprising: (a) any one of 1601 sequences (see ABP82019 to ABP83619) of 12-24 amino acids. Also described: (1) an assay for the detection of a particular G protein-coupled receptor (GPCR) or a candidate polypeptide in a sample; and (2) an isolated antibody having high specificity and high affinity or avidity for a particular GPCR. (I) can be used as GPCR modulators and in gene therapy. The antigenic peptides for GPCRs are useful in detecting an antibody against a particular GPCR, and in the production of specific antibodies. The peptides and antibodies are also useful for detecting the presence or absence of corresponding GPCRs. The antigenic peptides for GPCRs and antibodies are useful for diagnosing and designing drugs for treating immune-related diseases, growth-related diseases, cell regeneration-related disease, immunological-related cell proliferative diseases, or autoimmune diseases, e.g. AIDS, Alzheimer's disease, atherosclerosis, bacterial, fungal, protozoan or viral infections, osteoarthritis, osteoporosis, cancer, cardiomyopathy, chronic and acute inflammation, allergies, Crohn's disease, diabetes, graft versus host disease, Parkinson's disease, multiple sclerosis, pain, psoriasis, anxiety, depression, schizophrenia, dementia, mental retardation, memory loss, epilepsy, asthma, tuberculosis, obesity, nausea, hypertension, hypotension, renal disorders, rheumatoid arthritis, trauma, ulcers, or any other disorder in which GPCRs are involved. The antibodies may be used in immunoassays and immunodiagnosis. ABZ42523 to ABZ42869 encode GPCR proteins given in ABP81675 to ABP82018, which are used in the exemplification of the present invention
 CC Revised record issued on 15-JUN-2007 : Enhanced with precomputed information from BOND.
 SQ Sequence 907 AA;

Query Match 100.0%; Score 4702; DB 1; Length 907;
 Best Local Similarity 100.0%; Pred. No. 0;
 Matches 907; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 MDTSRGVLLSLPVLLQLATGGSSPRSGVLLRGCPTHCHCEPDGRMLLRVDCSDLGLSEL 60
 |||||||
 Db 1 MDTSRGVLLSLPVLLQLATGGSSPRSGVLLRGCPTHCHCEPDGRMLLRVDCSDLGLSEL 60

Qy 61 PSNLGVFTSYLDLSMNNISQLPNPLPSLRFLEELRLAGNALTYIPKGAFTGLYSLKVL 120

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Db      ||||||| 61 PSNL SVFTSYLDLSMNNISQLPNPLPSLRFLEELRLAGNALTYIPKGAF TGLYSLKVL 120
Qy      121 LQNNQLRHVPTEALQNLRLSLSLQSLRLDANHISYVPPSCFSGLHSLRHLWLDDNALTEIPVQ 180
Db      121 LQNNQLRHVPTEALQNLRLSLSLQSLRLDANHISYVPPSCFSGLHSLRHLWLDDNALTEIPVQ 180
Qy      181 AFRSL SALQAMTLALNKIHIPDYAFGNLSSIVVLHHLHNNRIHSLGKCFDGLHSLETLD 240
Db      181 AFRSL SALQAMTLALNKIHIPDYAFGNLSSIVVLHHLHNNRIHSLGKCFDGLHSLETLD 240
Qy      241 LNYNNLDEFPTAIRTLSNLKELGFHSNNI RSIPEKA FVG NPSLITIHFYDNPIQFVGRSA 300
Db      241 LNYNNLDEFPTAIRTLSNLKELGFHSNNI RSIPEKA FVG NPSLITIHFYDNPIQFVGRSA 300
Qy      301 FQH LPELRTLT LNGASQITEFPDLTG TANLESLT LTGAQISSLPQTVCNQLPNLQVLDLS 360
Db      301 FQH LPELRTLT LNGASQITEFPDLTG TANLESLT LTGAQISSLPQTVCNQLPNLQVLDLS 360
Qy      361 YNLLEDLPSFSVCQKLQKIDLRHNEIYEIKVDTFQQLLRLSRLNLAWNKIAIIHPNAFST 420
Db      361 YNLLEDLPSFSVCQKLQKIDLRHNEIYEIKVDTFQQLLRLSRLNLAWNKIAIIHPNAFST 420
Qy      421 LPSLIK LLDLSSNLLSSFPITGLHGLTHLKL TG NHALQSLISSENFP ELKVIEMPTYAYQCC 480
Db      421 LPSLIK LLDLSSNLLSSFPITGLHGLTHLKL TG NHALQSLISSENFP ELKVIEMPTYAYQCC 480
Qy      481 AFGVCENAYKISNQWNKGDNSSMDDLHKKDAGMFQAQDERDLEDFL LD FEEDL KALHSVQ 540
Db      481 AFGVCENAYKISNQWNKGDNSSMDDLHKKDAGMFQAQDERDLEDFL LD FEEDL KALHSVQ 540
Qy      541 CSPSPGPFKPCEHLLDGWLIRIGWWTIAVLALT CNALVTSTVFRS PLYI SPIKLLIGVIA 600
Db      541 CSPSPGPFKPCEHLLDGWLIRIGWWTIAVLALT CNALVTSTVFRS PLYI SPIKLLIGVIA 600
Qy      601 AVNMLTGVSSAVLAGVDAFTFGSFARHGAWWENGVGCHVIGFLSIFASESSVFLTLAAL 660
Db      601 AVNMLTGVSSAVLAGVDAFTFGSFARHGAWWENGVGCHVIGFLSIFASESSVFLTLAAL 660
Qy      661 ERGFSVKYSAKFETKAPFSSLKVIILLCALLALTMAAVPLLGGSKYGASPLCLPLPFGE 720
Db      661 ERGFSVKYSAKFETKAPFSSLKVIILLCALLALTMAAVPLLGGSKYGASPLCLPLPFGE 720
Qy      721 STMGYMVALILLNSLCFLMMTIAYTKLYCNLDKG DLENIWDCSMVKHIA LLFTNCILNC 780
Db      721 STMGYMVALILLNSLCFLMMTIAYTKLYCNLDKG DLENIWDCSMVKHIA LLFTNCILNC 780
Qy      781 PVAFLSFSSLINLT FISPEVIKFILLVVVPLPA CLNP LLYI LFNP HFKE DLVSLR KQTYV 840
Db      781 PVAFLSFSSLINLT FISPEVIKFILLVVVPLPA CLNP LLYI LFNP HFKE DLVSLR KQTYV 840
Qy      841 WTRSKHPSLMSINSDDVEKQSCDSTQALVTFTSSSITYDLPSSVPSPAYPVTE SCHLSS 900
Db      841 WTRSKHPSLMSINSDDVEKQSCDSTQALVTFTSSSITYDLPSSVPSPAYPVTE SCHLSS 900
Qy      901 VAFVPC L 907
Db      901 VAFVPC L 907

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US-10-225-567A-422

; Sequence 422, Application US/10225567A
; Publication No. US20030113798A1
; GENERAL INFORMATION:
; APPLICANT: LifeSpan Biosciences
; APPLICANT: Brown, Joseph P.
; APPLICANT: Burmer, Glenna C.

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; APPLICANT: Roush, Christine L.
; TITLE OF INVENTION: ANTIGENIC PEPTIDES AND ANTIBODIES FOR G PROTEIN-COUPLED RECEPTORS (GPCRS)
; FILE REFERENCE: 1920-4-4
; CURRENT APPLICATION NUMBER: US/10/225,567A
; CURRENT FILING DATE: 2001-12-19
; PRIOR APPLICATION NUMBER: 60/257,144
; PRIOR FILING DATE: 2000-12-19
; NUMBER OF SEQ ID NOS: 2292
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 422
; LENGTH: 907
; TYPE: PRT
; ORGANISM: Homo sapiens
US-10-225-567A-422

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Qy	721 STMGYMVALILLNSLCFLMMTIAYTKLYCNLDKGDLENIWDCSMVKHIALLLFTNCILNC	780
Db	721 STMGYMVALILLNSLCFLMMTIAYTKLYCNLDKGDLENIWDCSMVKHIALLLFTNCILNC	780
Qy	781 PVAFLSFSSLINLTFISPEVIKFILLVVVPLPACLNPLLYILFNPHFKEDLVSLSRKQTYV	840
Db	781 PVAFLSFSSLINLTFISPEVIKFILLVVVPLPACLNPLLYILFNPHFKEDLVSLSRKQTYV	840
Qy	841 WTRSKHPSLMSINSDDVEKQSCDSTQALVFTSSITYDLPPSSVPSPAYPVTESCHLSS	900
Db	841 WTRSKHPSLMSINSDDVEKQSCDSTQALVFTSSITYDLPPSSVPSPAYPVTESCHLSS	900
Qy	901 VAFVPCL 907	
Db	901 VAFVPCL 907	

RESULT 2

US-10-703-145-8

; Sequence 8, Application US/10703145
; Patent No. 7056685
; GENERAL INFORMATION:
; APPLICANT: Chen, Jin-Long
; APPLICANT: Ling, Lei
; APPLICANT: Tian, Hui
; APPLICANT: Tularik Inc.
; TITLE OF INVENTION: Receptor Ligands and Methods of Modulating Receptors
; FILE REFERENCE: 018781-009040US
; CURRENT APPLICATION NUMBER: US/10/703,145
; CURRENT FILING DATE: 2003-11-05
; PRIOR APPLICATION NUMBER: US 60/424,093
; PRIOR FILING DATE: 2002-11-05
; NUMBER OF SEQ ID NOS: 19
; SOFTWARE: PatentIn Ver. 2.1
; SEQ ID NO 8
; LENGTH: 907
; TYPE: PRT
; ORGANISM: Homo sapiens
; FEATURE:
; OTHER INFORMATION: human LGR5 G-protein coupled receptor (GPCR)

US-10-703-145-8

Query Match 100.0%; Score 4702; DB 3; Length 907;
Best Local Similarity 100.0%; Pred. No. 0;
Matches 907; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1 MDTSRGVLLSLPVLLQLATGGSSPRSGVLLRGCPTHCHCEPDGRMLLRVDCSDLGLSEL	60
Db	1 MDTSRGVLLSLPVLLQLATGGSSPRSGVLLRGCPTHCHCEPDGRMLLRVDCSDLGLSEL	60
Qy	61 PSNLNSVFTSYLDLSMNNISQLLPNPLPSLRFLEELRLAGNALTYIPKGAFTGLYSLKVLM	120
Db	61 PSNLNSVFTSYLDLSMNNISQLLPNPLPSLRFLEELRLAGNALTYIPKGAFTGLYSLKVLM	120
Qy	121 LQNNQLRHVPTEALQNLRSLSQSLRDLANHISYVPPSCFSGLHSLRHLWLDDNALTEIPVQ	180
Db	121 LQNNQLRHVPTEALQNLRSLSQSLRDLANHISYVPPSCFSGLHSLRHLWLDDNALTEIPVQ	180
Qy	181 AFRSLSLQAMTLALNKIHIPDYAFGNLSSLVVLHHLHNNRIHSLGKKCFDGLHSLETLD	240
Db	181 AFRSLSLQAMTLALNKIHIPDYAFGNLSSLVVLHHLHNNRIHSLGKKCFDGLHSLETLD	240
Qy	241 LNYNNLDEFPTAIRTLSNLKELGFHSNNIRSipeKAfVGnPSLITIHfYDNPIQFVGRSA	300
Db	241 LNYNNLDEFPTAIRTLSNLKELGFHSNNIRSipeKAfVGnPSLITIHfYDNPIQFVGRSA	300

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Qy	301 FQHLPELRTLTLNGASQITEFPDLTGTANLESLTGTGAQISSLPQTVCNQLPNLQVLDLS 360
Db	301 FQHLPELRTLTLNGASQITEFPDLTGTANLESLTGTGAQISSLPQTVCNQLPNLQVLDLS 360
Qy	361 YNLLEDLPSFSVCQKLQKIDLRHNEIYEIKVDTFQQLLRLRSRLNLAWNKIAIIHPNAFST 420
Db	361 YNLLEDLPSFSVCQKLQKIDLRHNEIYEIKVDTFQQLLRLRSRLNLAWNKIAIIHPNAFST 420
Qy	421 LPSLIKLDLSSNLLSSFPITGLHGLTHLKLGNHALQSLISSENFPBKVIEMPTYAYQCC 480
Db	421 LPSLIKLDLSSNLLSSFPITGLHGLTHLKLGNHALQSLISSENFPBKVIEMPTYAYQCC 480
Qy	481 AFGVCENAYKISNQWNKGDNSSMDLHKKDAGMFQAQDERDLEDFLDFEEDLKALHSVQ 540
Db	481 AFGVCENAYKISNQWNKGDNSSMDLHKKDAGMFQAQDERDLEDFLDFEEDLKALHSVQ 540
Qy	541 CSPSPGPKPKCEHLLDGWLIRIGVWTIAVLALTNCALVTSTVRSPLYISPIKLLIGVIA 600
Db	541 CSPSPGPKPKCEHLLDGWLIRIGVWTIAVLALTNCALVTSTVRSPLYISPIKLLIGVIA 600
Qy	601 AVNMLTGVSAGLAGVDAFTFGSFARHGAWWENGVGCHVIGFLSIFASESSVFLLTLAAL 660
Db	601 AVNMLTGVSAGLAGVDAFTFGSFARHGAWWENGVGCHVIGFLSIFASESSVFLLTLAAL 660
Qy	661 ERGFSVKYSAKFETKAPFSSLKVIIILLCALLALTMAAVPLLGGSKYGASPLCLPLPFGEP 720
Db	661 ERGFSVKYSAKFETKAPFSSLKVIIILLCALLALTMAAVPLLGGSKYGASPLCLPLPFGEP 720
Qy	721 STMGYMVALILLNSLCFLMMTIAYTKLYCNLDKGDLENIWDCSMVKHIALLLFTNCILNC 780
Db	721 STMGYMVALILLNSLCFLMMTIAYTKLYCNLDKGDLENIWDCSMVKHIALLLFTNCILNC 780
Qy	781 PVAFLSFSSLINLTFISPEVIKFILLVVVPLPACLNPPLYILFNPHFKEDLVSRLRKQTYV 840
Db	781 PVAFLSFSSLINLTFISPEVIKFILLVVVPLPACLNPPLYILFNPHFKEDLVSRLRKQTYV 840
Qy	841 WTRSKHPSLMSINSDDVEKQSCDSTQALVTFTSSITYDLPSSVPSPAYPVTESCHLSS 900
Db	841 WTRSKHPSLMSINSDDVEKQSCDSTQALVTFTSSITYDLPSSVPSPAYPVTESCHLSS 900
Qy	901 VAFVPCL 907
Db	901 VAFVPCL 907

11. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday from 8:30 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chang-Yu Wang, Ph.D.
October 14, 2009

/Chang-Yu Wang/
Examiner, Art Unit 1649